



Docket No. 10914-11

CERTIFICATE OF MAILING

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Lauren Jessenden

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IN THE UNITED STATES PATENT & TRADEMARK OFFICE

Applicant: Isa Odidi et al : Paper No.:
Serial No. : 09/403,437 : Group Art Unit: 1615
Filed: October 21, 1999 : Examiner: A. Pulliam

For: **Controlled Release Formulations Using Intelligent Polymers**

SECOND DECLARATION UNDER 37 C.F.R. 1.132

Box Fee Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Isa Odidi and Amina Odidi declare that:

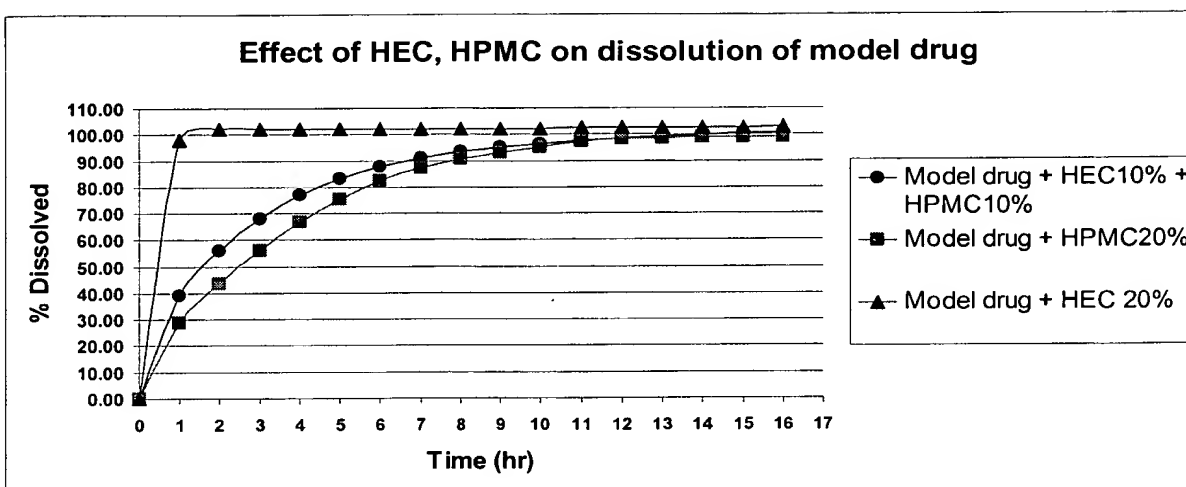
1. They are coinventors of and are familiar with the present U.S. Patent Application Serial No. 09/403,437, and they are familiar with the Official Actions issued in the present application and the references cited by the Examiner, including U.S. Patent No. 5,000,962 to Sangekar et al, U.S. Patent No. 5,162,117 to Stupak et al, and U.S. Patent No. 6,083,532 to Zhang et al.
2. In order to demonstrate significant and unexpected improvements exhibited by the controlled release pharmaceutical compositions and methods defined by claims 1, 14, 19, 23, 30, 33 and 34 in the present application, they conducted, or had conducted under their direction and control, certain experiments as described herein.

3. In one experiment, three compositions containing the same active agent were prepared and studied for their model drug release properties. The three compositions respectively contained (a) 10% hydroxypropylmethyl cellulose (HPMC) and 10% hydroxyethyl cellulose (HEC), (b) 20% HPMC, and (c) 20 % HEC. Composition (a) was therefore according to the teachings of the claimed invention, while compositions (b) and (c) were comparative in nature.

4. The rates of dissolution are set forth in the following table, in terms of release of the model drug:

Time, Hr	(a) Model drug + HEC10% + HPMC10%	(b) Model drug + HPMC20%	(c) Model drug + HEC 20%
0	0.00	0	0.00
1	39.05	28.83	98.15
2	56.18	43.76	102.10
3	68.05	56.01	102.28
4	76.92	66.73	102.09
5	83.42	75.56	102.11
6	87.88	82.38	102.18
7	91.08	87.19	102.18
8	93.43	90.61	102.19
9	95.17	93.28	102.20
10	96.55	95.36	102.32
11	97.66	97.11	102.55
12	98.59	98.32	102.49
13	99.33	98.59	102.55
14	99.90	98.94	102.77
15	100.38	98.93	102.69
16	100.73	98.93	102.83

5. These results are set forth graphically as follows:



6. These results show differences in rate of dissolution when the same drug is formulated with (a) a combination of 10% HEC and 10% HPMC, versus (b) 20% HEC, or (c) 20% HPMC. For example, at one hour, 39.05% of the model drug was released from composition (a) containing the HEC/HPMC combination, while only 28.83% of the model drug was released from the composition (b) containing only HPMC, yet 98.15% was released from composition (c) containing only HEC. These differences in dissolution rates are significant, especially with high potency drugs where both immediate and delayed release are necessary. Particularly, composition (a) according to the invention provides improved early dosing over composition (b) and improved delayed dosing over composition (c).

7. The improved model drug release profile exhibited by composition (a) as compared with compositions (b) and (c) is neither taught nor suggested by any of Sangekar et al, Stupak et al, and Zhang et al, as these references do not teach any of HPMC, HEC or combinations of HPMC and HEC as having any differences in drug release profiles.

8. Isa Odidi and Amina Odidi further declare that all statements made herein of his/her own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both,



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under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Respectfully submitted,

December 3, 2003

December 3, 2003

Len Odidi

Amina Odidi